

Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see [Authors & Referees](#) and the [Editorial Policy Checklist](#).

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a Confirmed

- ☒ The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
- ☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- ☒ The statistical test(s) used AND whether they are one- or two-sided
Only common tests should be described solely by name; describe more complex techniques in the Methods section.
- ☒ A description of all covariates tested
- ☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- ☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
- ☒ For null hypothesis testing, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
Give P values as exact values whenever suitable.
- ☒ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- ☒ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- ☒ Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection no custom software was used

Data analysis no custom software was used

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research [guidelines for submitting code & software](#) for further information.

Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author (S.H.) on reasonable request.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

- ☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	For ethical considerations, the group size of animal experiments is small. For transmission studies, groups of 8 ferrets per virus were used: four donor ferrets and four recipient ferrets. The results of the transmissions studies are qualitative, i.e the identification of the virus genotype that was transmitted, rather than quantitative, and no comparison between the viruses was necessary to draw the conclusions. Therefore, no sample size calculation was performed. Moreover, no comparison of the transmission efficacy of the different viruses, which would require more animals per group for statistical analysis, was performed. For pathogenesis studies, groups of three ferrets per virus and per time point were used. The outcome of these experiment is semi-quantitative. Because of the small sample size, no statistical analysis was performed and only trends are discussed.
Data exclusions	No data were excluded from the analyses
Replication	For the transmission studies, data were replicated by having four independent transmission experiments per virus (see sample size). For pathogenesis studies, data were replicated by having three independent infection experiments per virus. In vitro-experiments were performed in biological duplicates.
Randomization	Ferrets were randomly allocated to each group.
Blinding	Investigators were blinded while performing the virus titration, the analyses of the next-generation sequencing and the scoring of immunochemistry analyses.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Human research participants
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data

Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Antibodies

Antibodies used	mouse IgG2a anti-influenza A nucleoprotein, H16-L10-4R5 (ATCC® HB-65™);mouse IgG2a, MAB003, R&D Systems;goat anti-mouse IgG2a coupled to horseradish peroxidase (HRP), Biorad, Star133P
Validation	The mouse IgG2a anti-influenza A nucleoprotein was used according to the manufacturer instructions. For the isotype control, the same amount of antibody as the primary antibody was used.

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	American Type Culture Collection and Epithelix Sarl
Authentication	None of the cell lines were authenticated
Mycoplasma contamination	All cell lines tested negative for mycoplasma
Commonly misidentified lines (See ICLAC register)	None of the cell lines used in this study have been identified as commonly misidentified lines

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals	Mustela putorius furo, female, 6-month old
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Wild animals

the study did not involve wild animals

Field-collected samples

the study did not involve samples collected from the field

Ethics oversight

Independent animal experimentation ethical review committee ‘stichting DEC consult’

Note that full information on the approval of the study protocol must also be provided in the manuscript.